REMARKS/ARGUMENTS

Patent Office Interview

On November 18, 2004, the Undersigned Attorney was granted a personal interview with Patent Office representative including Examiner Jeffrey Fredman, Group 1600 Quality Assurance Specialist Deborah Reynolds and Group 1600 Director Jasemine Chambers. The focus on the interview was the orientation of the disclosed oligonucleotide CTCGGTACCTACTGG. Applicants' Attorney agreed to provide an amendment specifying the oligonucleotide polarity, and a Substitute Sequence Listing. The possibility of providing a Declaration Under 37 CFR 1.132 by an expert skilled in the art to which the invention applies was also discussed. Applicants have identified a qualified candidate who is currently studying the underlying documentation. Should additional evidence be required, Applicants will be in a position to provide this evidence.

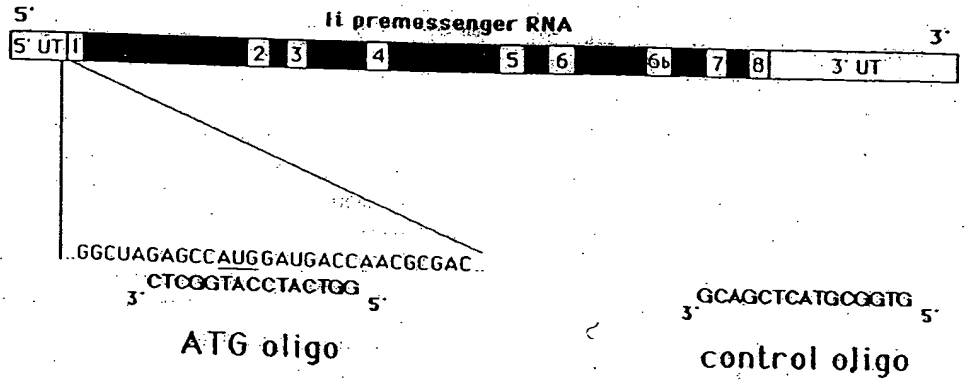
Claim Interpretation

Page 3 of the Office Action discusses the issue of polarity of an oligonucleotide disclosed in Fig. 2 of Bertolino et al. (*Int. Immunol.* 3: 435-443 (1991)). The Office Action states that:

> The Sequence Rules, specifically 37 CFR 1.822(c)(5), note "A nucleotide sequence shall be presented, only by a single strand, in the 5 to 3 direction, from left to right. Therefore, SEQ ID NO: 1 is not the same oligonucleotide as that used in the Bertolino et al. (International Immunol. (1991) 3(5): 435-443) reference at figure 2, which is 5'GGTCATCCATGGCTC3' ...

Applicants' Attorney has concurrently submitted a Declaration Under 37 CFR 1.132 addressing the issue of polarity in the Sequence Listing, and arguments relating to this are provided below. However, Applicants must take issue with the above-quoted language as it highlights the fact that presentation in the 5' to 3' orientation is not universal. Contrary to the statement of the Patent Office, Bertolino Fig. 2 does not disclose the oligonculeotide 5'GGTCATCCATGGCTC3'. Rather, Fig. 2 from the cited reference (reproduced below) discloses the oligonculeotide 3'CTCGGTACCTACTGG5'. This presentation highlights the fact that presentation in the 5' to 3'

orientation is not universal and 3' to 5' orientation is frequently used when presenting antisense oligonucleotide sequences.



Rejection Under 35 USC 102

Claims 97-100 have been rejected under 35 USC 102(b) as being anticipated by Bertolino et al. (*Int. Immunol.* 3: 435-443 (1991)). This rejection is respectfully traversed. At the time that priority US Application No. 09/205,995 was filed on December 4, 1998, no polarity was specifically assigned to the disclosed oligonucleotide CTCGGTACCTACTGG. The oligonucleotide was disclosed in 3 locations in the priority application as filed: on page 7, in Claim 1 and in Claim 50. At these 3 locations the oligonucleotide was described in such a way as to make clear that it is a specific regulator of Ii protein expression. The priority application exemplifies two classes of such regulators of Ii protein expression – antisense molecules and reverse gene constructs. It would be clear and unambiguous to one skilled in the art that the disclosed oligonucleotide CTCGGTACCTACTGG is an antisense molecule designed to hybridize specifically to an RNA molecule encoding mammalian Ii protein (see, for example, Claim 3 as filed in the priority application). The Sequence Listing specifically identifies the oligonucleotide of SEQ ID NO: 1 as an "antisense oligonculeotide corresponding to a specific region of the mouse Ii gene".

The prior art at the time that the priority application was filed included limited disclosure of Ii protein sequence which was readily searchable for complementarity. Among the prior art disclosures was Koch et al., EMBO J. 6: 1677-1683 (1987)). The Koch et al. reference discloses the murine Ii gene sequence. The oligonucleotide 3'-CTCGGTACCTACTGG-5' is

perfectly complementary with the sequence 5'-GAGCCATGGATGACC-3' shown in Fig. 2 of the Koch et al. reference which is located a the 5' end of the gene sequence starting 5 nucleotides upstream of the ATG codon.

While it is true that oligonucleotides are conventionally presented in the 5'- 3' orientation, antisense oligonucleotides are frequently presented in the 3' – 5' orientation (as was the case in the Bertolino et al. reference on which the statement of rejection is grounded). Based on the requirement that the oligonucleotide CTCGGTACCTACTGG must be complementary with a mammalian Ii mRNA, it would be immediately apparent to one skilled in the art that the polarity as presented was in the 3' – 5' orientation. Executed Declarations signed by the three inventors, perfecting the filing of the priority application were filed with the Patent Office on January 8, 1999.

Almost two years after the executed Declarations were filed, Applicants' Attorney prepared and filed a response to a Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures (paper filed November 6, 2000). The filing included a request to amend the Specification by incorporating an attached Sequence Listing. SEQ ID NO: 1 is shown as ctcggtacctactgg which corresponds to the order of nucleotides as shown elsewhere in the Specification. However, the rules governing the preparation and filing of a Sequence Listing indicate that the order of nucleotides should be presented in the 5' – 3' direction. Thus, Applicants' Attorney, by the submission of the Sequence Listing, inadvertently added new matter to the application in contradiction to the following statement which was included with the filing:

> Applicants' Attorney hereby states that the above amendments to the Specification and Claims include no new matter.

A Declaration by Applicants' Attorney stating facts relating to the preparation and filing of the Sequence Listing on January 6, 2000 is attached. Prior to the introduction of the Sequence Listing, Applicant had not specified a polarity and, as indicated above, it would be clear to one of skill in the art that the polarity was necessarily 3' – 5' because the other possible polarity would describe an oligonucleotide which is not complementary to mammalian Ii mRNA.

In light of the error introduced by Applicants' Attorney approximately two years after the application was filed, Applicant is preparing a Substitute Sequence Listing for entry in the

present application as a supplemental paper. The only change in the Substitute Sequence Listing over that presently of record is the reversal of the polarity of the oligonucleotide of SEQ ID NO: 1. This change does not represent the addition of new matter – to the contrary, the entry removes from the application new matter which was inadvertently added during the prosecution of the parent application approximately two years after it was filed.

It is respectfully submitted that the evidence provided herein, together with the amendment to the Specification, is sufficient to overcome the rejection under 35 USC 102.

Rejection Under 35 USC 103

Claims 97-100 have been rejected under 35 USC 103(a) as being unpatentable over Bertolino et al. (*Int. Immunol.* 3: 435-443 (1991)), in view of Koch et al. (EMBO J. 6: 1677-1673 (1987), and further in view of either Bennett et al. (US Patent No. 5,514,788), Anderson et al. (US Patent No. 5,422,049) and Cowsert et al. (US Patent No. 5,945,290). More specifically, the Patent Office states on page 5 that:

> Bertolino teaches a method for displaying an autodeterminant peptide (see abstract), in association with a MHC class II protein, on the surface of a MHC class II-positive antigen presenting cell ...

This rejection is respectfully traversed. As discussed at page 2, lines 12-15 of the Specification as filed:.

> Under normal conditions, endogenous peptides (with self determinants potentially leading to autoimmune disease) are not bound to MHC class II molecules since the Ii protein is always cosynthesized with nascent MHC class II molecules.

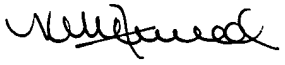
Applicants' pending claims are directed toward methods for displaying such autodeterminant peptides in association with an MHC Class II protein on the surface of an MHC class II-positive cell. Contrary to the statement in the Office Action on page 5, Bertolino does not teach a method for displaying an autodeterminant peptide. Nothing in the cited Bertolino et al. reference discloses or suggests that it is possible to present such autodeterminant peptides in association with an MHC Class II protein on the surface of an MHC class II-positive cell. Bertolino et al. investigated the role of Ii in the presentation of hen egg lysozyme (HEL) and measles virus

hemaglutinin (HA) antigens to MHC class II-restricted T hybridoma cells. Neither of these antigens can be described as comprising or containing "autodeterminant peptides". Likewise, the proposed combination of references fails to cure this deficiency in the Bertolino et al. reference.

Summary

In light of the above amendment, consideration of the subject patent application is respectfully requested. Any deficiency or overpayment should be charged or credited to Deposit Account No. 500282.

Respectfully submitted,



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